

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
24 June 2004 (24.06.2004)

PCT

(10) International Publication Number
WO 2004/052904 A3

(51) International Patent Classification⁷: **C07H 17/00**,
A61K 31/70, A61P 31/04

(21) International Application Number:
PCT/HR2003/000062

(22) International Filing Date:
10 December 2003 (10.12.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
P20020991A 12 December 2002 (12.12.2002) HR

(71) Applicant (for all designated States except US): **PLIVA**
- **ISTRAZIVACKI INSTITUT D.O.O.** [HR/HR]; Prilaz
baruna Filipovica 29, 10000 Zagreb (HR).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **KUJUNDZIC**,
Nedjeljko [HR/HR]; Slavenskog 4, 10000 Zagreb (HR).
BUKVIC, Krajacic, Mirjana [HR/HR]; Tjardoviceva
28, 10000 Zagreb (HR). **BRAJSA**, Karmen [HR/HR];
Jablanska 42, 10000 Zagreb (HR).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC,
SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (BW, GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the International search report:
2 September 2004

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: NOVEL SEMISYNTHETIC MACROLIDE ANTIBIOTICS OF THE AZALIDE SERIES

(57) Abstract: The invention relates to N"-substituted 9a-N-(N'-carbamoyl-γ-aminopropyl), 9a--N-(N'-thiocarbamoyl-γ-amino-
propyl), 9a-N-[N'-((β-cyanoethyl)-N'-carbamoyl-γ-aminopropyl)] and 9a-N-[N'-((β-cyanoethyl)-N'-thiocarbamoyl-γ-aminopropyl)]
derivatives of 9-deoxo-9-dihydro-9a-aza-9a-homoerithromycin A and 5-O-desosaminyl-9-deoxo-9-dihydro-9a-aza-9a-ho-
moerithronolide A, novel semisynthetic macrolide antibiotics of the azalide series, of the general formula 1, wherein R represents
H or cladinosyl moiety, R¹ represents H or (β-cyanoethyl) moiety, R² represents isopropyl, 1-naphtyl, 2-naphtyl, benzyl,
2-(trifluoromethyl)phenyl, 3-phenylpropyl, β-phenylethyl, ethoxycarbonylmethyl, 1-(1-naphtyl)ethyl, 3,4,5-trimethoxyphenyl and
2,4-dichlorophenyl group, and X represents O and S, and their acceptable addition salts thereof with inorganic or organic acids, to
the process for preparation of their pharmaceutical compositions as well as the use their compositions in the treatment of bacterial
infections.

WO 2004/052904 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/HR 03/00062

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07H17/00 A61K31/70 A61P31/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07H A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 492 688 A (BRIGHT GENE M) 8 January 1985 (1985-01-08) claim 9	1-56
A	WO 97/35590 A (PLATT CHRIS E) 2 October 1997 (1997-10-02) claim 4	1-56
A	EP 0 132 944 A (PFIZER) 13 February 1985 (1985-02-13) claim 1	1-56



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- * & * document member of the same patent family

Date of the actual completion of the international search

21 June 2004

Date of mailing of the international search report

02/07/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Bardili, W

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/HR 03/00062

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 4492688	A	08-01-1985	DE 3461803 D1	05-02-1987
			DK 249984 A ,B,	19-12-1984
			EP 0132026 A1	23-01-1985
			GR 82038 A1	12-12-1984
			IE 57509 B1	07-10-1992
WO 9735590	A	02-10-1997	WO 9735590 A1	02-10-1997
EP 0132944	A	13-02-1985	US 4464527 A	07-08-1984
			DE 3461805 D1	05-02-1987
			DK 319884 A ,B,	31-12-1984
			EP 0132944 A1	13-02-1985
			GR 79536 A1	30-10-1984
			IE 57564 B1	16-12-1992
			JP 60025998 A	08-02-1985